REMARKS

In this Amendment, Applicant has cancelled Claims 1 – 36 without prejudice or disclaimer and added Claims 37 – 54. Claims 37 – 54 have been added to specify different embodiments of the present invention and overcome the rejection. It is respectfully submitted that no new matter has been introduced by the new claims. All claims are now present for examination and favorable reconsideration is respectfully requested in view of the preceding amendments and the following comments.

REJECTIONS UNDER 35 U.S.C. § 112 FIRST PARAGRAPH:

Claims 1 – 16 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

It is respectfully submitted that the new claims have overcome the rejection and satisfy the written description requirement. More specifically, new Claim 37 is directed to a recombinant fusion polypeptide comprising a fusion protein partner which "consists of a TolAIII domain defined by the amino acid sequence of SEQ ID NO: 13", which is sufficiently supported by the specification. In addition, new Claim 54, which depends on Claim 37, recites that the fusion protein partner may be "a functional homologue, functional fragment or functional derivative of the TolAIII domain defined by the amino acid sequence of SEQ ID NO: 13". The Applicant submits that the specification adequately describes this genus of fusion protein partner for the following reasons.

At first, the specification describes on page 2, lines 23 – 26 that various homologues of the TolA protein are known in the art, including those from *E. coli*, *Salmonella* species, *Pectobacterium* species and *Haemophilus* species. As would be understood by one skilled in the relevant art, these homologues of TolA each possess in their structure a TolAIII domain equivalent to the TolAIII domain of *E. coli* (as provided in SEQ ID NO: 13). These equivalent TolAIII domains of TolA homologues are included in the claimed TolAIII homologues. The specification further discloses that each

homologue of TolAIII domain encompassed by the invention must be a functional homologue. The biological function of the fusion protein partner is to ensure higher levels of expression in a host cell of a non-TolA polypeptide attached to the fusion protein partner compared with expression of the non-TolA polypeptide lacking the fusion protein partner (as now recited in new claim 37; and see for example specification at page 2, lines 28-30 and page 27, last paragraph). An assay to determine such activity is disclosed in the specification (see for example Materials and Methods section, pages 15-17). Therefore, the specification teaches the skilled reader that the TolAIII domain homologues of the invention have both a structural and functional (or biological) relationship with the *E. coli* TolAIII domain.

In addition, the claimed genus of fusion protein partner in Claim 54 encompasses a functional fragment or a functional derivative of the *E. coli* TolAIII domain. These members of the genus firstly have the above-mentioned functional or biological characteristic of the TolAIII domain. On a structural level, these members are also derived or derivable from the TolAIII domain in ways that would be clear to one skilled in the relevant art. For example, the derivative may include amino acid analogs which are well known. Alternatively, the derivative may be a sequence of amino acids which differs from the *E. coli* TolAIII domain sequence in that one or more amino acids within the base sequence are substituted for other amino acids. A fragment of the *E. coli* TolAIII domain would simply be one in which amino acid residues had been deleted from the N- and/or C-terminus. Therefore, a structural relationship between the *E. coli* TolAIII domain and a fragment or derivative thereof is apparent.

In summary, Applicant respectfully submits that the genus of the claimed fusion protein partner in Claim 54 is adequately described in the specification, in such a way that one skilled in the relevant art would understand that the inventors had possession of the claimed invention.

With regard to the Examiner's rejection of previous Claim 1 as containing new matter and being indefinite due to the phrase "basic structure, in sequence, ...", the

Applicant submits that the Examiner has misunderstood this phrase in the context of the specification (see page 3, lines 20-24). As a person of ordinary skill in the art would read this phrase, it would clearly mean not "basic" in the pH sense but "basic" is the sense of "essential" or "fundamental". In any event, this terminology has been removed in the new Claim 37 and dependent claims.

Therefore, the rejection under 35 U.S.C. § 112, first paragraph has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 112 SECOND PARAGRAPH:

Claims 1 – 13 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is respectfully submitted that the currently presented amendments clearly point out and define the embodiment of the present invention. More specifically, Claims 1 – 13 have been cancelled. Thus, the rejection to these claims is moot. It is respectfully submitted that, in the new Claims 37 – 54 clearly define the invention. More specifically, the term "a basic structure" has been deleted.

In addition, the terms "TolAIII" and "BCL-XL" have been defined by specific sequences. Applicant respectfully submits that these terms are not "laboratory designations" but abbreviations used by those skilled in the art to designate the respective protein domain and protein. Nevertheless, Applicant has inserted SEQ ID NOs as requested by the Examiner in order to define the amino acid sequences (see new Claims 37 and 51). With reference to Claim 51, the amino acid sequence of BCL-XL has been added and identified as SEQ ID NO: 62 (see amended Sequence Listings). This sequence has been obtained from SWISSPROT Accession No. B47537, which is disclosed on page 4, lines 29-30 of the specification. Therefore, no new matter has been introduced. In a telephone conversation with the Examiner on January 31, 2007, the Examiner clarified

that the sentences on page 7, line 3 of the Office Action refers to the term "TolAIII". It is respectfully submitted that these terms have been defined by sequence numbers as indicated above.

Furthermore, the terms "optionally", "such as", "preferably" and "for example" have been deleted. The new claims properly cited relevant sequences.

Therefore, the rejection under 35 U.S.C. § 112, second paragraph, has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 101:

Claims 1 – 13 have been rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter.

It is respectfully submitted that in view of the currently presented amendments, the rejection has been overcome. More specifically, the pending claims define "recombinant" fusion polypeptides.

Therefore, the rejection under 35 U.S.C. § 101 has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 101 is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 102:

Claims 1 and 11 – 12 have been rejected under 35 U.S.C. § 102 (b) as allegedly being anticipated by WO 01/21817.

Applicant traverses the rejection and respectfully submits that the rejection is incorrect and the present-claimed invention is not anticipated by the cited reference. More specifically, WO01/21817 teaches a genetically modified bacteriophage, pseudovirion or phagemid which is capable of entering a host cell by specific binding to

an artificial receptor, preferably via an artificial ligand (page 4, line 26 to page 5, line 4). In one aspect, the bacteriophage, pseudovirion or phagemid is used to identify interacting proteins (page 7, lines 11-13). Here, a host cell may be modified to express on its surface a bait or prey species for interaction with a corresponding prey or bait species displayed on the bacteriophage, pseudovirion or phagemid (page 7, lines 14-20). WO01/21817 teaches one embodiment where "TolA is used as fusion partner for the display of bait or prey on the surface of said *E. coli* strains" (page 7, lines 26-27; emphasis added). The function of TolA as disclosed in WO01/21817 thus requires that the TolA fusion partner is anchored to the cell surface for display of bait or prey.

A co-inventor of the present invention, Professor Jeremy Lakey (School of Cell and Molecular Biosciences, University of Newcastle Upon Tyne, UK), has observed that the use of TolA in WO01/21817 as a fusion partner upon which to add an artificial cell surface receptor relies upon largely intact TolA or a TolA protein comprising at least TolA domains I and II but excluding the TolAIII domain, because it is the TolA domains I and II that are required to anchor the fusion to the surface of the *E. coli* strains used. It is stated in WO01/21817 on page 8, lines 1-2 that having the TolA-fusion at the C-terminus end of TolA "may result in the deletion of a smaller or lager *(sic)* part of TolA". The person of ordinary skill in the art would appreciate that this teaches that TolA domain III could be deleted, not domains I and II because if these two domains were deleted this would leave only the TolAIII domain which is, on its own, cytoplasmic and cannot act as the basis for a cell surface receptor as required in WO01/21817. To confirm this observation, it is respectfully submitted that WO01/21817 discloses on page 8, lines 4 to 7 a specific embodiment in which the "D1-binding domain of TolA has been deleted and replaced by the fusion partner". This D1-binding domain corresponds to the TolAIII domain (as shown in Riechmann & Holliger, 1997, Cell 90: 351-360; of record). Thus, WO01/21817 teaches that their fusion protein lacks a TolAIII domain but includes domains I and II of TolA.

Therefore, the use of the TolA protein as disclosed in WO01/21817 relies upon surface exposure of the fusion partner attached to a complete TolA protein or a protein

comprising the TolA domains I and II but excluding the TolAIII domain. This is in contrast to the presently claimed invention where the only part of TolA used as fusion protein is the TolAIII domain. Thus, WO01/21817 fails to disclose the presently claimed fusion polypeptide in which only the TolAIII domain of TolA, and not domains I and II of TolA, are used as fusion protein partner for linking to a non-TolA polypeptide.

Furthermore, because it is essential, according to WO01/21817, that the TolA fusion partner is attached to the surface of *E. coli* strains, there is no disclosure or teaching that the TolA protein or any part thereof can be used as a fusion protein partner to facilitate higher levels of expression in a host cell of a non-TolA polypeptide linked thereto. This functional feature, and Claim 37 and its dependent claims as a whole, are not anticipated by WO01/21817.

Therefore, the newly presented claims are not anticipated by WO01/21817 and the rejection under 35 U.S.C. § 102 (b) has been overcome. Accordingly, withdrawal of the rejection under 35 U.S.C. § 102 (b) is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 103:

Claims 2 – 4 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over WO01/21817 in view of Wan et al. Claims 5 – 8 have been rejected under 35 U.S.C. §103 as allegedly being unpatentable over WO01/21817 in view of Mai et al. (U.S. Pat. No. 5,087,564). Claim 8 – 10 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over WO01/21817 in view of Derouiche et al. Claim 13 has been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over WO01/21817 in view of Mark et al. (US Pat. Pub. No. 2002/0137049).

Applicant traverses the rejection and respectfully submits that the embodiments of present-claimed invention are not obvious over the cited references. More specifically, With regard to the Examiner's rejection of Claims 2-4 under 35 USC 103 over WO01/21817 in view of Wan (1998), the Applicant notes that WO01/21817 fails to disclose the recombinant fusion polypeptide as claimed for reasons cited above.

Combining Wan with WO01/21817 does not remedy this deficiency because Wan does not teach a recombinant fusion polypeptide in which the TolAIII domain is located towards the N-terminus and is combined with a non-TolA polypeptide towards the C-terminus.

With regard to the Examiner's rejection of Claims 5-8 under 35 USC 103 over WO01/21817 in view of Mai (US5,087,564), Applicant respectfully submits that WO01/21817 fails to disclose the recombinant fusion polypeptide as claimed for reasons cited above. Combining Mai with WO01/21817 does not remedy this deficiency because Mai does not teach a recombinant fusion polypeptide in which the TolAIII domain is located towards the N-terminus and is combined with a non-TolA polypeptide towards the C-terminus.

With regard to the Examiner's rejection of Claims 8-10 under 35 USC 103 over WO01/21817 in view of Derouiche (1997), Applicant respectfully submits that WO01/21817 fails to disclose the recombinant fusion polypeptide as claimed for reasons cited above. Combining Derouiche. with WO01/21817 does not remedy this deficiency because Derouiche *et al.* does not teach a recombinant fusion polypeptide in which the TolAIII domain is located towards the N-terminus and is combined with a non-TolA polypeptide towards the C-terminus.

Furthermore, regarding with regard to the Examiner's rejection of Claim 13 under 35 USC 103 over WO01/21817 in view of Mark (US2002/0137049), Applicant respectfully submits that WO01/21817 fails to disclose the recombinant fusion polypeptide as claimed for reasons cited above. Combining Mark with WO01/21817 does not remedy this deficiency because Mark does not teach a recombinant fusion polypeptide in which the TolAIII domain is located towards the N-terminus and is combined with a non-TolA polypeptide towards the C-terminus.

Finally, Applicant respectfully submits that none of the cited prior art teaches or suggests to a person of ordinary skill in the art that the TolAIII domain, when separated

from domains I and II of the TolA protein and fused with a non-TolA polypeptide in the orientation as defined in Claim 37, would allow for enhanced expression in a host cell of the non-TolA polypeptide fused thereto. WO01/21817 teaches away from the present invention by specifying that their fusion protein preferably lacks the TolAIII domain. Therefore, the remarkable properties of the TolAIII domain as a fusion protein partner, as demonstrated for the first time by the present inventors, would not have been obvious to one of ordinary skill in the art.

In summary, the amended and newly presented claims are not obvious over the cited references. The rejection under 35 U.S.C. § 103 has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 103 is respectfully requested.

Having overcome all outstanding grounds of rejection, the application is now in condition for allowance, and prompt action toward that end is respectfully solicited.

Respectfully submitted,

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